

Definition

Infrequently, patients will note enlarged lymph nodes and present with the chief complaint of having a nodule, a swollen gland, a “knot,” or enlarged lymph nodes; more commonly, patients do not recognize that they have significantly enlarged lymph nodes, and the lymphadenopathy is discovered by the physician. Since lymphadenopathy can be associated with a wide range of disorders spanning relatively benign medical problems such as streptococcal pharyngitis to life-threatening diseases such as malignancies, the discovery of enlarged nodes represents an important physical finding that demands a systematic evaluation.

Technique

In searching for lymph nodes, one must be gentle; otherwise, lymph nodes that are only minimally enlarged or embedded in tissue may not be apparent. Particular attention should be directed to the size, shape, and consistency of enlarged nodes. Lymph nodes that are smooth and relatively soft, but slightly enlarged, may be normal and reveal only hyperplasia when biopsied. Enlarged lymph nodes that have an irregular shape and a rubbery, hard consistency may be infiltrated by malignant cells. Tender nodes are suggestive of an inflammatory process. Matted nodes or nodes fixed to underlying structures should raise the question of malignancy or infection; freely movable nodes are more likely to occur in benign conditions.

The extent and location of lymphadenopathy are important in determining and providing diagnostic clues to the cause of lymphadenopathy. All major lymph node chains should be evaluated in a systematic fashion. Begin with a visual inspection of the area, looking for asymmetry or erythema. Palpate in a systematic fashion, encompassing all accessible lymph nodes. For an examination of lymph nodes of the neck, the patient either sits or stands facing the examiner. The examiner’s right hand explores the left side of the patient’s neck and then the left hand of the examiner explores the right side of the patient’s neck. Starting from the top of the neck and going down, all of the various cervical lymph node chains should be evaluated including the preauricular, posterior auricular, occipital, superior cervical, posterior cervical, submaxillary, submental, inferior deep cervical, and supraclavicular, as noted in Figure 149.1. In the absence of generalized adenopathy, enlargement of specific cervical lymph node groups can be helpful diagnostically. For example, posterior auricular adenopathy suggests rubella, whereas unilateral anterior auricular adenopathy is associated with lesions of the conjunctiva and eyelids with the resultant oculoglandular syndrome seen in trachoma, tularemia, cat-scratch fever, tuberculosis, syphilis, epidemic keratoconjunctivitis, and outbreaks of adenovirus type 3 pharyngoconjunctival fever. Oropharyngeal

and dental infections can also cause cervical adenopathy. Bilateral cervical adenopathy is also prominent in tuberculosis, coccidioidomycosis, infectious mononucleosis, toxoplasmosis, sarcoid, lymphomas, and leukemias. However, a unilateral cervical mass that is firm and nontender should always raise the question of an undetected nasopharyngeal carcinoma.

Supraclavicular adenopathy is almost always abnormal. When it is not part of generalized lymphadenopathy, it is suggestive of a primary malignancy in either the abdomen or the chest. Right-sided supraclavicular nodes drain parts of the lung and mediastinum and are signals of intrathoracic lesions, particularly in the lung and esophagus. Left-sided supraclavicular nodes, which carry the eponym “Virchow’s nodes,” are close to the thoracic duct and often signal intra-abdominal tumors, particularly from the stomach, ovaries, testes, or kidneys. Supraclavicular nodes are sometimes deep seated, and it is often helpful to have the patient perform a Valsalva maneuver in order to push the cupola of the lung upward, thereby bringing these deep-seated nodes to a more accessible position for palpation. If supraclavicular adenopathy is noted, the patient should also be closely examined for hilar and mediastinal adenopathy. Although a chest x-ray or computerized tomography is often needed to verify this type of lymphadenopathy, dullness to percussion over the manubrium is sometimes suggestive of an anterior mediastinal mass or mediastinal nodes.

The patient should then be examined for axillary adenopathy. The patient may be either sitting or supine. The

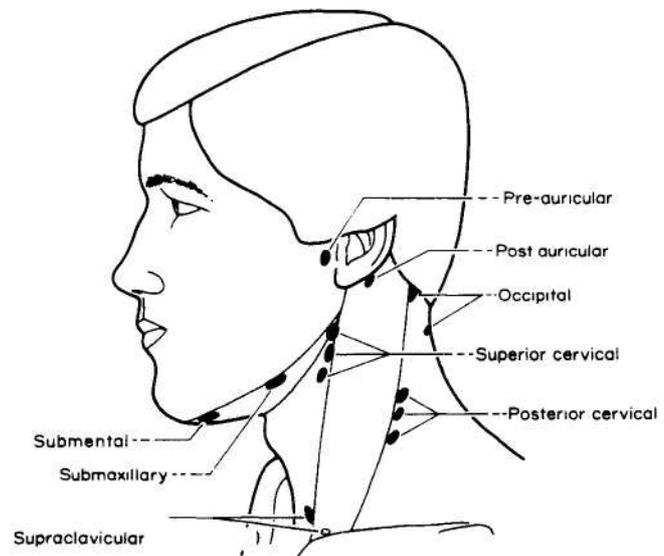


Figure 149.1
Lymph node locations in the neck.

patient's arm, supported by one of the examiner's hands, should be held in a slightly flexed position and adducted. The examiner's right hand is used to examine the patient's left axilla, and the left hand for the right axilla, as shown in Figure 149.2A. The examiner's fingers should be slightly cuffed and should reach as high into the apex of the axilla as possible. Fingers are brought down slowly, exerting gentle pressure against the thorax. This maneuver should be repeated several times in order to examine the lateral group, the medial group, and the pectoral group of axillary nodes. Axillary adenopathy may be part of a generalized process or may be localized and secondary to infection in the limb. Local infection or trauma causing the adenopathy should be searched for carefully. Concomitant epitrochlear, axillary, and supraclavicular adenopathy should raise the question of cat-scratch fever. In a female, unilateral axillary nodes raise the suspicion of an ipsilateral breast carcinoma.

Next, the patient should be evaluated for the possibility of epitrochlear nodes. Often, these nodes are overlooked, or inadequate techniques are employed to examine them. Epitrochlear nodes are best sought with the patient's elbow flexed to about 90°. The right epitrochlear area is approached by inserting the examiner's left hand from behind the patient's elbow while the examiner's right hand grasps the right wrist of the patient, supporting the forearm, as in Figure 149.2B. The fourth and fifth finger should fall just above the medial epicondyle of the humerus and then the other fingers will overlie the area where epitrochlear nodes are usually found. Examination of the left epitrochlear area is just the reverse of the right. Epitrochlear nodes are usually enlarged secondary to infections of the hand and forearm. Occasionally, neoplastic processes will present with isolated epitrochlear adenopathy. Enlarged epitrochlear

nodes occur frequently in mononucleosis. In the past, epitrochlear lymphadenopathy was considered a diagnostically important sign of secondary syphilis, but now it is more commonly due to recurrent hand injury or infections in people who do manual labor.

Occasionally, lymph nodes can be found in the vicinity of the umbilicus. These nodes have the eponym "the node of Sister Mary Joseph" and are a signal of significant intra-abdominal lymphadenopathy, usually associated with malignant processes.

The inguinal region should be carefully evaluated for significant lymphadenopathy. It is not uncommon for adults to have what has been termed "shotty" nodes in the inguinal region. These shotty nodes are usually firm, not fixed, and are less than a centimeter in diameter. They result from recurrent infections and insults to the feet and legs. Significantly enlarged and tender nodes in the inguinal region that are not part of generalized lymphadenopathy should suggest a variety of conditions including syphilis, chancroid, and lymphogranuloma venereum. Unilateral inguinal lymphadenopathy is usually a response to infection of an ipsilateral lower extremity. Inguinal adenopathy can also be part of systemic processes such as lymphoma or leukemia.

Femoral adenopathy is usually located in the femoral triangle in the area of the node of Cloquet. Although femoral adenopathy can also be secondary to chronic infection and trauma, it is much more commonly of pathologic significance than is inguinal adenopathy.

Occasionally lymphadenopathy can be found in the popliteal fossa. This adenopathy can be part of a generalized process or can be localized secondary to infection or trauma of the lower extremity.

Many important lymph node groups cannot be evaluated

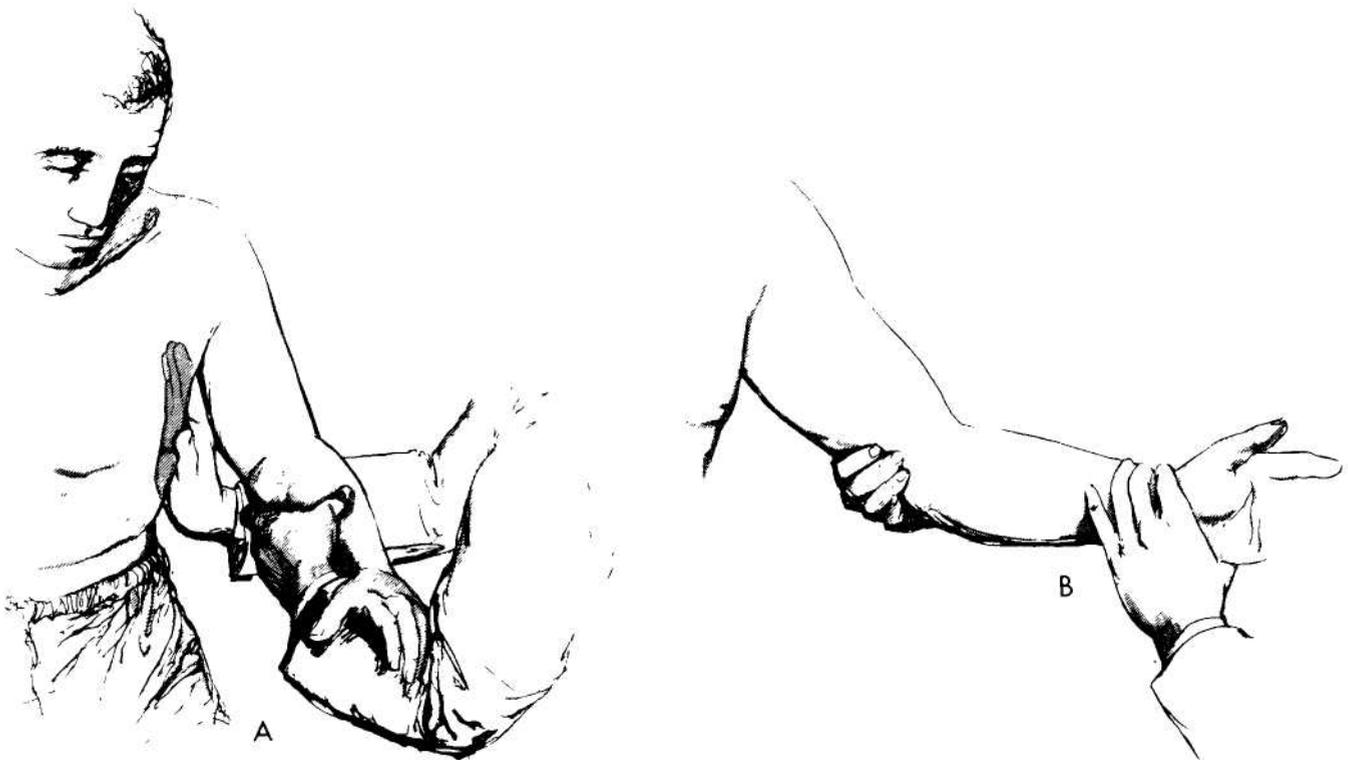


Figure 149.2

(A) Technique for palpation of axillary nodes. (B) Technique for palpation of epitrochlear lymph nodes. (From Judge RD, Zuidema GD, eds. *Physical diagnosis: a physiologic approach*. Boston: Little, Brown, 1963; 225.)

by the physical examination. Whenever there is evidence of generalized adenopathy, these groups should be evaluated carefully. Hilar and mediastinal adenopathy can compromise regional structures such as the superior vena cava or trachea and potentially cause a life-threatening complication.

There are multiple lymph node groupings in the abdomen, including mesenteric, paraaortic, celiac, and retrogastric. Bulky abdominal adenopathy can also compromise structures, including the ureters and inferior vena cava, and can cause complications such as renal failure. Abdominal adenopathy is usually evaluated by computerized abdominal tomography, gallium scanning, ultrasonography, or lymphangiography.

The spleen is part of the lymphatic system and should be carefully evaluated in any patient in whom other lymphadenopathy is present.

Basic Science

There are over 500 lymph nodes gathered in a variety of groupings throughout the body. These nodes represent an integral part of both the immunologic and reticuloendothelial systems. Individual lymph nodes consist of lymphocytes clustered in lymphoid follicles and reticuloendothelial cells lining nodal sinuses. Each follicle contains a germinal center populated by rapidly proliferating B cells and macrophages. The germinal center is surrounded by densely packed small lymphocyte T cells that replicate at a slower rate. Both B and T cells function in the recognition of, and response to, antigenic stimulation. B cells are the principal effector cells of the humoral arm of the immune system, whereas T cells are the principal effector cells of the cellular arm of the immune system. Macrophages and cells of the reticuloendothelial system are also part of the immunologic system, but function in the phagocytosis of cellular debris or foreign substances such as viruses and bacteria that have gained access to the node from the area being drained. The reticuloendothelial system also clears some excess metabolites from the circulation.

The enlargement of lymph nodes, either localized or generalized, can be the consequence of several different pathologic mechanisms. Lymphadenopathy may represent an increase in the number and size of lymphoid follicles with proliferation of lymphocytes as a response to a new antigen. There can be enlargement of lymph nodes with infiltration of the node by cells normally not present, such as metastatic tumor or leukemic cells. Lymphadenopathy can occur secondary to unknown stimuli that cause normal cells to become transformed to lymphoma cells and to proliferate autonomously. Lymph nodes can be infiltrated by polymorphonuclear cells, a condition called *lymphadenitis*, or lymph nodes can be infiltrated by macrophages laden with metabolites, as in lipid storage diseases.

Clinical Significance

Given the mechanisms by which lymph nodes enlarge, it is clear that the differential diagnosis of lymphadenopathy involves infectious processes, immunologic conditions, malignant processes, storage diseases, and a variety of miscellaneous disorders (Table 149.1).

Information from the clinical history is invaluable in the diagnostic management of the patient with lymphadenop-

Table 149.1
Conditions Causing Lymphadenopathy

Infections

Localized: a response to a local infection such as streptococcal pharyngitis

Generalized: a response to a systemic infection such as tuberculosis, syphilis, infectious mononucleosis, hepatitis, fungal infection, toxoplasmosis, HIV, etc.

Immunologic conditions

Known antigens such as drug reactions or serum sickness

Unknown antigens such as in sarcoidosis

Connective tissue disease such as rheumatoid arthritis, systemic lupus erythematosus

Miscellaneous: giant lymph node hyperplasia, dermatopathies, lymphadenitis, immunoblastic lymphadenopathy

Malignant processes

Diffuse involvement, as in lymphomas and leukemias

Diffuse invasion, as in diffuse carcinomatosis

Localized invasion, as in head and neck tumors

Lipid storage diseases

Miscellaneous

Graves' and Addison's diseases

athy, and frequently leads to an accurate diagnosis without the need for extensive diagnostic testing. The age of the patient is quite important. Dramatic enlargement of lymph nodes and other lymphoid tissue such as the adenoids and tonsils is often a normal response to a variety of relatively weak antigenic stimuli such as mild viral and bacterial infections or vaccinations in infants and children, whereas in adults these antigens will not elicit a generalized response. This age difference in the expression of lymphadenopathy is of such importance as to warrant an almost totally different diagnostic approach to patients before and after puberty.

Specific inquiries should be made about drugs, allergies, animal exposures, hobbies, and occupation. Lymphadenopathy as an adverse response to drugs and allergies is well recognized. Exposure to cats may raise a question of cat-scratch fever in a patient who presents with unilateral lymphadenopathy of an extremity. Enlarged, nontender lymph nodes in the epitrochlear, axillary, femoral, and inguinal areas are often seen in patients with occupations in which recurrent, usually minor, injuries to extremities occur. Generalized lymphadenopathy also can occur in patients with such chronic dermatologic disorders as eczema. If acquired immune deficiency syndrome (AIDS) is suspected, information must be obtained concerning potential risk factors for this disorder: sexual preference, contact with individuals with the disorder, transfusion of blood products, etc.

Information must also be obtained about the lymphadenopathy itself. Tender, painful nodes that appear and enlarge within a few days to a few weeks are most often secondary to an inflammatory process in the area drained by the lymph nodes. Occasionally a patient with tender, rapidly enlarging lymphadenopathy will have lymphoma or leukemia. However, slowly growing, nontender nodes may be indicative of either local or generalized malignancy.

A careful history must be taken regarding constitutional symptoms including fever, night sweats, weight loss, pruritus, and generalized malaise. These symptoms can be associated with either malignancies or infectious processes such as tuberculosis or hepatitis.

Specific symptoms such as cough may raise the question of tuberculosis or fungal pulmonary infection; a history of jaundice or clay-colored stools should raise the question of hepatitis. Usually any diagnosis or condition suggested by the history requires corroboration by data from the physical examination and appropriate laboratory tests or lymph node biopsy. Infectious processes can be localized, as in a response to a local abscess or to cellulitis. When the infection is systemic in nature, the lymphadenopathy is also usually generalized, as in tuberculosis, brucellosis, infectious mononucleosis, hepatitis, fungal infections, and toxoplasmosis.

Immunologic conditions that cause lymphadenopathy can be secondary to clearly identified antigens, as in serum sickness, or a response to an insect bite, or the lymphadenopathy may be secondary to antigenic stimulation in conditions where the antigen has not been identified. Examples of the latter include the connective tissue disorders including rheumatoid arthritis and systemic lupus erythematosus. Sarcoidosis is another example of an immunologic process that causes widespread lymphadenopathy, although the causative antigen has not yet been identified.

A recently recognized viral (HIV) cause of lymphadenopathy is a systemic infection causing severe immunologic deficiencies in the host. This syndrome has been labeled the AIDS complex. Unexplained generalized adenopathy should raise the possibility of AIDS or AIDS-related complex, and the individual should be carefully evaluated for possible risk factors. Blood samples for viral titers should also be obtained.

Invasion by malignant cells can cause either regional lymphadenopathy, as in patients with head and neck tumors, or generalized lymphadenopathy, as in patients with disseminated carcinomatosis. Lymphoma can also result in either regional or generalized lymphadenopathy.

Generalized lymphadenopathy may also be the result of a variety of other conditions, including Gaucher's disease, Graves' disease, and Addison's disease.

In most patients with lymphadenopathy, a diagnosis can be made after a careful history, physical examination, and appropriate testing including hematologic parameters, ser-

ologic tests, skin tests, and routine x-rays. As in all diagnostic work-ups, these tests should be performed in a goal-directed manner in order to evaluate specific hypotheses. If a specific diagnosis cannot be established after appropriate evaluation, but infection is suspected, cautious observation after appropriate cultures have been obtained may be warranted. Indiscriminate use of antibiotics for unsubstantiated infections should not be encouraged. On the other hand, if the diagnosis cannot be established and a malignancy is a major concern, biopsy of a lymph node is appropriate and should be done in a timely fashion. When a biopsy is done, adequate tissue should be obtained for both histologic examination and appropriate cultures. Occasionally, more than one node may have to be biopsied in order to determine the appropriate diagnosis. Occasionally, nodes will reveal only non-specific lymphoid hyperplasia, whereas a neighboring node will harbor metastatic tumor. If an inadequate specimen is obtained, the malignant disease may not be diagnosed.

In conclusion, although the differential diagnosis of lymphadenopathy may be broad and sometimes initially confusing, the careful gathering of data from the history, physical, and appropriate laboratory tests will resolve the differential in the vast majority of patients.

References

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